

Laboratory Testing and the Thrombophilia Workup

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Roles of the Clinical Laboratory

- Useful ancillary data for initial diagnosis (d-dimer).
- Monitoring antithrombotic therapy.
- Evaluation for underlying hypercoagulable state(s).
 - Identifies individuals 'at risk' for thrombosis.
 - Identifies individuals with an initial thrombosis who are at higher risk for recurrence.

What laboratory tests are useful in the *acute* setting?

- D-dimer ◇ supportive data to help rule out venous thromboembolism.
- Troponins/BNP ◇ stratify severity of PE.
- PT, aPTT ◇ essential baseline information prior to starting therapy.
- Hypercoagulable workup generally *not* useful in the acute setting.

Who should be considered for thrombophilia testing?

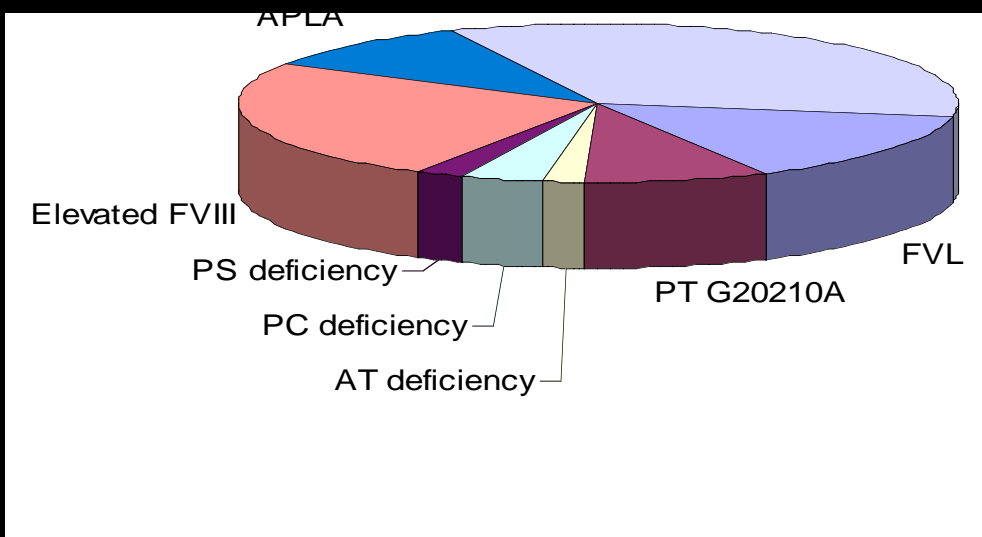
- Patients with unexplained, or 'idiopathic' thromboembolism.
- Patients with thromboembolism that is unusual, extensive, or in an unusual location (e.g., portal vein thrombosis).
- Patients with a striking family history for venous thromboembolism.

What tests should be done?

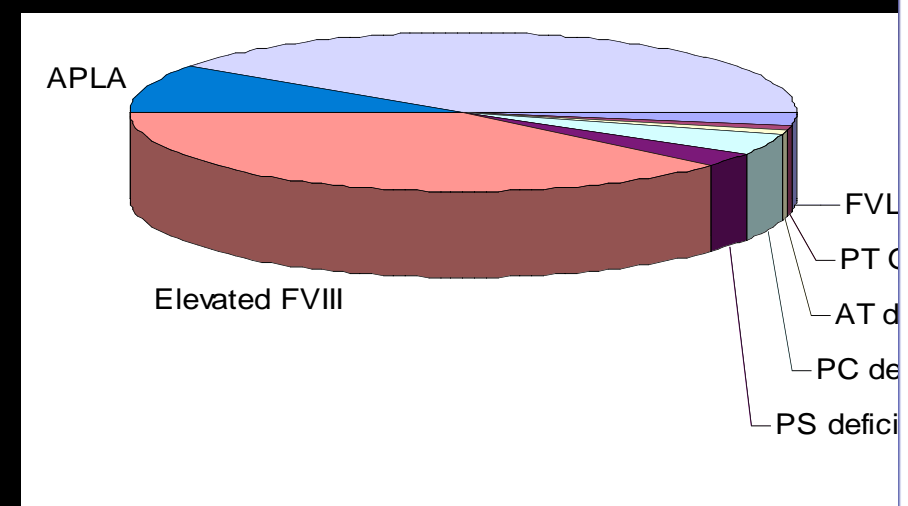
- Activated protein C resistance, with analysis for factor V Leiden if positive.
- Prothrombin G20210A genotype analysis.
- Antithrombin functional assay.
- Protein C functional assay.
- Protein S functional assay, with antigenic assays if indicated.
- Antiphospholipid antibody testing.
- Homocysteine level.
- Factor VIII assay.

Thrombophilic states and race

Caucasian

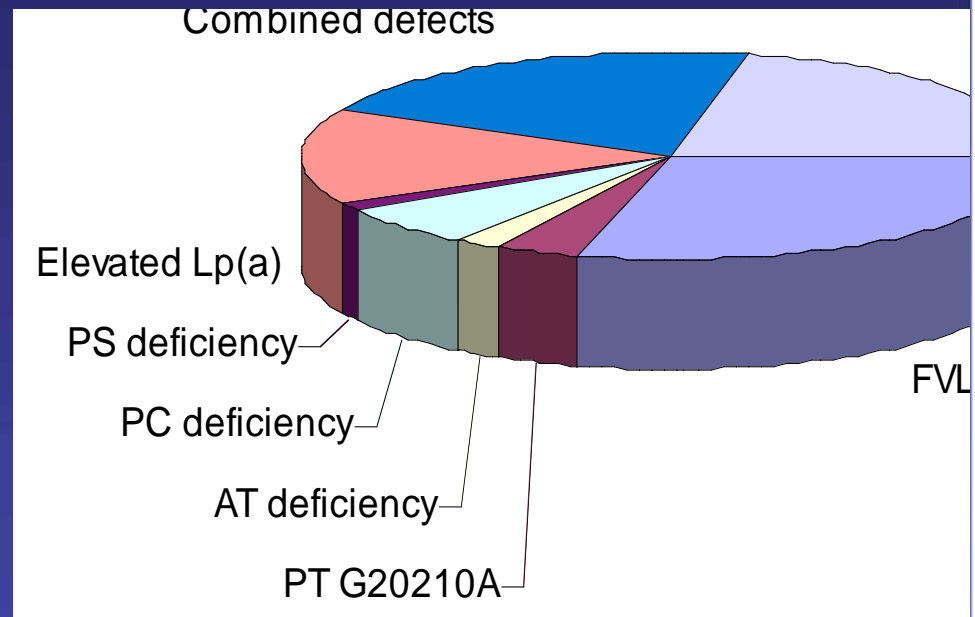


African-American



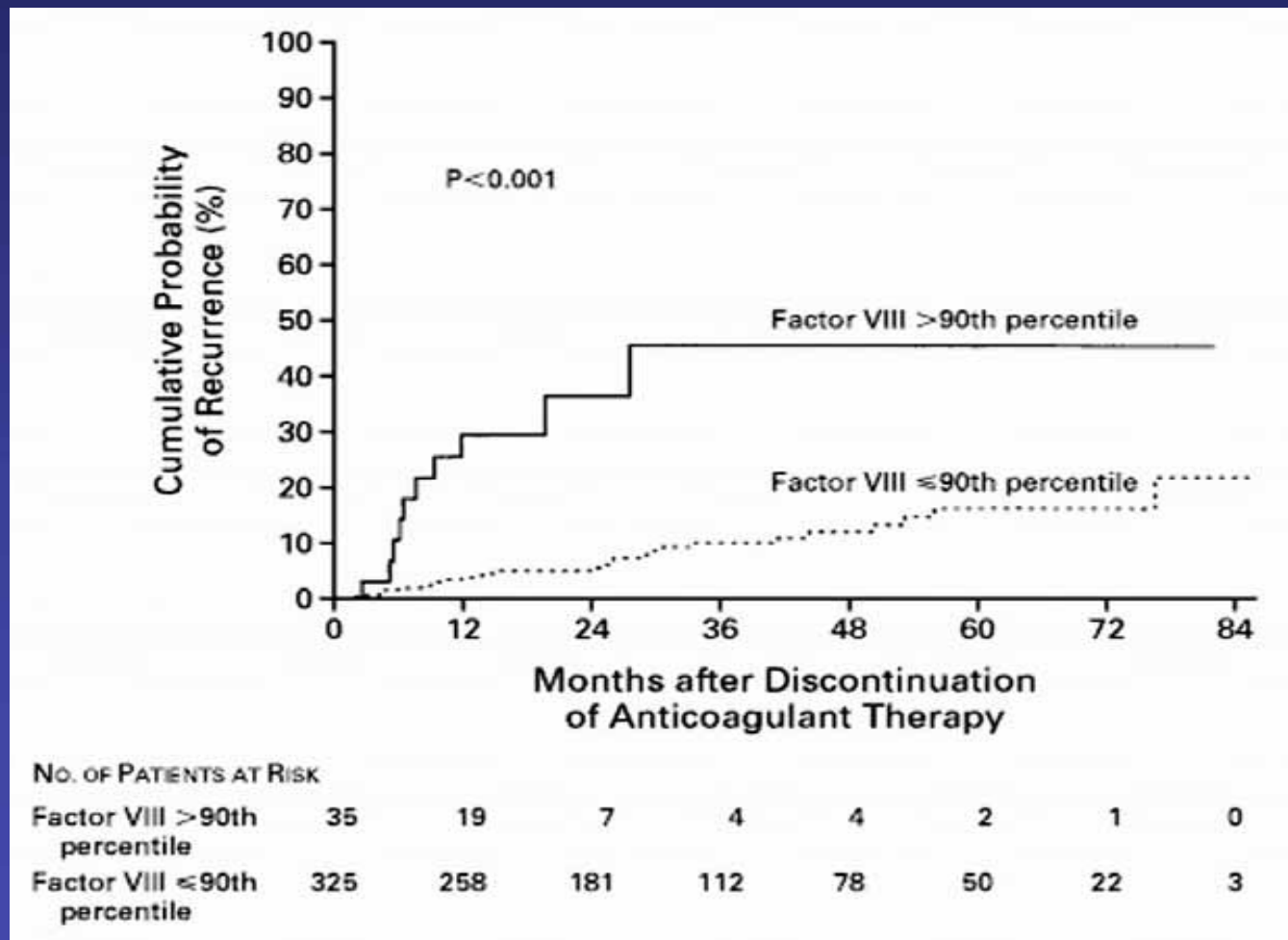
Thrombophilia in the pediatric patient

- Many studies include children with central venous lines and other acquired disorders.
- Elevated factor VIII and D-dimer is also associated with recurrent thrombosis



Age: neonate to

Impact of thrombophilic disorders on recurrent thromboembolism



Kyrle, P. A. *et al.* N Engl J Med 2000; 343:457-462. © 2000 Massachusetts Medical Society. All rights reserved.

ACCP Guidelines

2.1.4. For patients with first episode DVT and:

- Antiphospholipid antibodies;
- 2 or more thrombophilic conditions;

◇ therapy for 12 months (1C+) or indefinite (2C+)

2.1.5. For patients with first episode DVT and:

- Antithrombin, protein C or protein S deficiency;
- Factor V Leiden or prothrombin G20210A;
- Elevated homocysteine or factor VIII levels

◇ therapy for 6-12 months (1A) or indefinite (2C+)

Cost of thrombophilia testing

Test	Approximate Cost*
Natural anticoagulants (antithrombin, protein C, protein S):	\$450-750
Genetic tests (factor V Leiden, prothrombin G20210A):	\$600
Antiphospholipid antibodies:	\$1000-1500
Other (factor VIII, homocysteine):	\$200
TOTAL:	\$2250-3050

* Duke Coagulation Lab

What should healthcare providers do with this information?

- Individuals who test positive for a thrombophilic risk factor require counseling as to:
 - risks of thrombosis to themselves *and their family members*.
 - importance of early recognition of signs and symptoms of venous thromboembolism.
 - risks and benefits of thromboprophylaxis in high-risk situations.

Should asymptomatic individuals be screened for thrombophilia?

- Screening of asymptomatic individuals, whether family members of a patient with thrombosis, or in a situation that places them at increased risk for thrombosis, is generally not recommended.
- However, in selected situations, knowledge of a specific thrombophilic state might guide therapeutic decision-making (e.g., decision concerning HRT usage).

On the other hand,
one doesn't even
need the doctor to
order the test...



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Future directions for thrombophilia testing

- Prospective clinical studies to define:
 - Role, if any, of screening asymptomatic family members or individuals in high-risk situations.
 - Impact on optimal therapy for patients with venous thrombosis and thrombophilia.
- Better education for providers as well as consumers concerning risk factors, prevention strategies, need for genetic counseling, *etc.*